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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/758,717	01/16/2004	James R. Dasch	1733.1068-008	6559

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EXAMINER	
RUSSEL, JEFFREY E	

ART UNIT	PAPER NUMBER
1654	

DATE MAILED: 03/31/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/758,717	DASCH ET AL.	
	Examiner	Art Unit	
	Jeffrey E. Russel	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 January 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *16 January 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *20040706;20041115*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

1. The disclosure is objected to because of the following informalities: The status of the U.S. non-provisional patent applications at page 1, lines 3-5, and at page 16, line 24, needs to be updated. Appropriate correction is required.

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 8 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. There is no original disclosure supporting the recitation in claim 8 that the concentration of the bisphosphonate is from about 0.5% (w/w) to about 20% (w/w) of the total weight of the composition. While this numerical range is used to describe the concentration of biologically active agents in the composition (see page 9, line 18 - page 10, line 3), the bisphosphonate is a component separate and distinct from the biologically active agents (see, e.g., page 5, lines 25-28). Note that while this claim limitation occurs in a preliminary amendment to the application, the preliminary amendment does not form part of the original disclosure of the application because the application was filed with a copy of the declaration filed in the parent application. See MPEP 714.01(e)(II).

3. Claims 1, 2, and 8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 1 recites that R_2 can be H. However, "H" is a

monovalent atom. It is not clear to what the substituent Y is attached when R_2 is H. Claim 1 recites that R_2 can be N. However, "N" is a trivalent atom. It is not clear what occupies the third valence of N when R_2 is N.

4. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-8 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-58 of U.S. Patent No. 6,558,702. Although the conflicting claims are not identical, they are not patentably distinct from each other. The '702 patent claims sustained release compositions and their uses in which the bisphosphonate can be alendronate, risendronate, pamidronate, etidronate, or tiludronate (see, e.g., claim 49), and wherein the sustained release composition can be in the form of microparticles (see, e.g., claim 50), but does not explicitly claim the combination of the two, and does not claim a bisphosphonate concentration. It would have been obvious to one of ordinary skill in the art to form sustained release compositions as claimed in the '702 patent in which the bisphosphonate is alendronate, risendronate, pamidronate, etidronate, or tiludronate and wherein the sustained release composition is in the form of microparticles because these are preferred claimed embodiments of the '702 patent and because the resulting compositions have only the expected

sustained release activity. It would have been obvious to one of ordinary skill in the art to determine all operable and optimal bisphosphonate concentrations for the claimed compositions of the '702 patent because concentration is an art-recognized result-effective variable which is routinely determined and optimized in the pharmaceutical arts.

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

For the purposes of this invention, the level of ordinary skill in the art is deemed to be at least that level of skill demonstrated by the patents in the relevant art. Joy Technologies Inc. v. Quigg, 14 USPQ2d 1432 (DC DC 1990). One of ordinary skill in the art is held accountable not only for specific teachings of references, but also for inferences which those skilled in the art may reasonably be expected to draw. In re Hoeschele, 160 USPQ 809, 811 (CCPA 1969). In

addition, one of ordinary skill in the art is motivated by economics to depart from the prior art to reduce costs consistent with desired product properties. In re Clinton, 188 USPQ 365, 367 (CCPA 1976); In re Thompson, 192 USPQ 275, 277 (CCPA 1976).

6. Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by the D'Souza et al article (Drug Development and Industrial Pharmacy, Vol. 25, pages 591-596). The D'Souza et al article teaches clodronate, a bisphosphonate embraced by Applicants' Formula I, microencapsulated in crosslinked albumin microspheres. The albumin is biodegradable. The clodronate microspheres are administered to rats in order to block macrophage infiltration into the glomerulus in experimental glomerulonephritis. See, e.g., the Abstract; page 592, column 1; page 593, paragraph bridging columns 1 and 2; and Figure 3. Because of the presence of the crosslinked biodegradable albumin, the microsphere composition of the D'Souza et al article is inherently a sustained release composition.

7. Claim 8 is rejected under 35 U.S.C. 103(a) as being obvious over the D'Souza et al article (Drug Development and Industrial Pharmacy, Vol. 25, pages 591-596). Application of the D'Souza et al article is the same as in the above rejection of claim 1. The D'Souza et al article does not teach Applicants' claimed bisphosphonate concentrations. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to determine all operable and optimal clodronate concentrations for the microsphere compositions of the D'Souza et al article because concentration is an art-recognized result-effective variable which is routinely determined and optimized in the pharmaceutical arts.

8. Claims 1-4 and 8 are rejected under 35 U.S.C. 103(a) as being obvious over the European Patent Application 839,525. The European Patent Application '525 teaches sustained release preparations comprising a polymer of lactic acid and preferably about 0.1 to 30% (w/w) of a

physiologically active substance which can be a bone resorption suppressor such as alendronate and risendronate. See, e.g., the Abstract; page 5, lines 4-5; page 9, line 36; and page 9, line 52 - page 10, line 2. The European Patent Application '525 does not specifically exemplify a sustained release preparation comprising alendronate or risendronate, and does not teach the bisphosphonate concentration recited in instant claim 8. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to form sustained release preparations according to the European Patent Application '525 in which the physiologically active substance is alendronate or risendronate because the European Patent Application '525 specifically names alendronate and risendronate as physiologically active substances which can be usefully administered using the disclosed preparations. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to determine all operable and optimal alendronate and risendronate concentrations for the above-outlined preparations because concentration is an art-recognized result-effective variable which is routinely determined and optimized in the pharmaceutical arts.

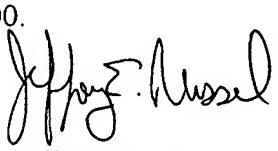
9. Claims 5-7 are rejected under 35 U.S.C. 103(a) as being obvious over the European Patent Application 839,525 as applied against claims 1-4 and 8 above, and further in view of Asgharnejad et al (U.S. Patent No. 6,123,964) or Bechard (U.S. Patent No. 5,431,920). The European Patent Application '525 teaches bone resorption suppressors in general as physiologically active substances which can be included in the sustained release preparations, but do not teach pamidronate, etidronate, or tiludronate specifically. Asgharnejad et al (see column 11, lines 15-30) and Bechard (see column 1, lines 25-55) teach that pamidronate, etidronate, and tiludronate are known pharmaceutical agents used to inhibit bone resorption and

to prevent osteoporosis. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to include the pamidronate, etidronate, or tiludronate of Asgharnejad et al or Bechard as the physiologically active substance in the sustained release preparations of the European Patent Application '525 because the European Patent Application '525 is not limited to any particular physiologically active substance, because the pamidronate, etidronate, and tiludronate are functionally and structurally closely related to the alendronate and risendronate which are disclosed by the European Patent Application '525, and because administering the pamidronate, etidronate, or tiludronate of Asgharnejad et al or Bechard in the form of the sustained release preparations of the European Patent Application '525 would have the benefit of release for at least about 5 months.

10. The European Patent Application 709,085 has been carefully considered but is not deemed to teach or suggest the instant claimed invention. The bisphosphonate which is present in the microcapsules of Example 10 of the European Patent Application '085 does not anticipate or suggest bisphosphonates having the Formula I as is recited in the instant claims. MacLean et al (U.S. Patent No. 5,773,477) has been carefully considered but is not deemed to teach or suggest the instant claimed invention. MacLean et al do not teach or suggest their compositions in the form of biodegradable microparticles.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey E. Russel at telephone number (571) 272-0969. The examiner can normally be reached on Monday-Thursday from 8:30 A.M. to 6:00 P.M. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Bruce Campell can be reached at (571) 272-0974. The fax number for formal communications to be entered into the record is (571) 273-8300; for informal communications such as proposed amendments, the fax number (571) 273-0969 can be used. The telephone number for the Technology Center 1600 receptionist is (571) 272-1600.



Jeffrey E. Russel

Primary Patent Examiner

Art Unit 1654

JRussel

March 28, 2005